

Integrated Gastric Acidity to Evaluate Acid Suppression With Proton Pump Inhibitor Therapy: A Five-Way Crossover Comparison

Philip B. Miner, Jr., MD¹; Yusong Chen, PhD²; Mark B. Sostek, MD³
¹Oklahoma Foundation for Digestive Research, University of Oklahoma Health Sciences Center, Oklahoma City, OK; ²Clinical Science, AstraZeneca LP, Wilmington, DE

CONCLUSIONS

- Esomeprazole provided significantly greater gastric acid suppression at steady state during most of the 24-hour time period than all other proton pump inhibitors as documented by levels of integrated gastric acidity.

1. BACKGROUND

- Integrated gastric acidity is a pharmacodynamic parameter that estimates the absolute reduction in gastric acidity with acid inhibitory therapy over time.
- Integrated gastric acidity considers both duration and magnitude of changes in intragastric hydrogen ion concentration that occur during a 24-hour period compared with percent time pH > 4.0 or other pH thresholds assessing the inhibitory effects of acid-suppressive agents.
- Integrated gastric acidity allows more complete and real-time characterization of the pharmacodynamic effects of acid-suppressive therapies, and potentially provides a more clinically relevant method for comparing such therapies.
- Effective acid-suppressive therapy should sufficiently reduce intragastric hydrogen ion concentration to optimize healing of acid-related upper gastrointestinal mucosal damage.

2. OBJECTIVE

- To evaluate acid suppression with each of the five available proton pump inhibitors by calculating integrated gastric acidity from 24-hour intragastric pH data.

3. METHODS

- A randomized, open-label, comparative 5-way crossover study was conducted comparing standard doses of once-daily oral esomeprazole 40 mg, omeprazole 20 mg, lansoprazole 30 mg, pantoprazole 40 mg and rabeprazole 20 mg.¹
- Patients were randomly assigned to receive one of five dosing sequences and must have completed all five treatment periods to be considered evaluable.
- Study drug was administered once daily on 5 consecutive mornings, 30 minutes prior to a standardized breakfast.
- Each treatment period was separated by a 10- to 17-day washout period during which no proton pump inhibitor was taken.
- Eligible participants included men and women aged 18 to 60 years with heartburn for an average of at least 2 days per month during the 2 months prior to screening. Patients with >3 episodes of heartburn per week during the 3 months prior to study entry were evaluated via esophagogastroduodenoscopy to rule out gastrointestinal pathology. Patients with previous or existing endoscopic evidence of esophageal erosions, ulcer or any other significant gastrointestinal pathology were excluded.

Table 1. Baseline Demographics and Clinical Characteristics (Evaluable Cohort; N = 34)

Female gender, n (%)	26 (76.5)
Age, y, mean (SD)	44.1 (11)
Caucasian race, n (%)	31 (91.2)
Height, cm, mean (SD)	167.6 (8.5)
Weight, kg, mean (SD)	83.2 (18.1)
Body mass index, kg/m ² , mean (SD)	29.4 (5.1)
Heartburn ≥3 times/week, n (%)	23 (67.6)

- Intragastric pH data was collected over 24 hours on day 5 of dosing with an intragastric pH probe positioned 10 cm below the anatomically located lower esophageal sphincter, with results summed cumulatively every 4 seconds and analyzed for each hour over a 24-hour period.²
- Integrated gastric acidity was calculated using the method of Gardner et al.²
- The data presented were obtained as part of a retrospective analysis.

4. RESULTS

- Baseline demographics and clinical characteristics of the 34 evaluable patients are summarized in the Table.

- The mean cumulative integrated gastric acidity for each of the five proton pump inhibitors in the 34 evaluable patients on day 5 is shown in the Figure. Lower levels of integrated gastric acidity correspond to higher degrees of acid suppression.

- Although this analysis was not designed to show a difference between comparators, the P value between esomeprazole and all other comparators was <0.05 for a majority of the hourly time points.

Integrated Gastric Acidity

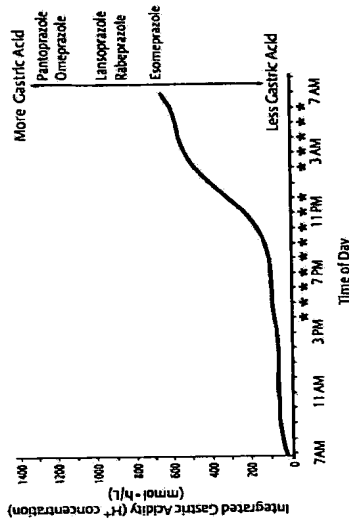


Figure. Mean cumulative integrated gastric acidity on day 5 (N = 34). * $P < 0.05$ for comparison between esomeprazole and all other comparators.

5. REFERENCES

1. Miner PB, Kuo PO, Chen Y, Jensen M. Esomeprazole 40 mg provides more effective intragastric acid suppression at steady state than standard doses of other proton pump inhibitors. *Gastroenterology*. 2003;124(3):679.
2. Gardner JD. Measurement of gastric acidity. *Am J Gastroenterol*. 1981;94(5):1483-1476.

Supported by a grant from AstraZeneca LP, Wilmington, DE, USA